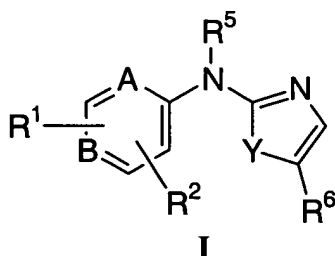


Amendments to the Claims:

This listing of claims will replace the current set of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A compound of Formula I



or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

A and B are independently N or $N^+ - O^-$;

Y is O, S or N-R⁴;

R^1 and R^2 are independently:

- 1) H,
- 2) $\text{O}_r(\text{C}_1\text{-C}_6)\text{perfluoroalkyl}$,
- 3) OH,
- 4) CN,
- 5) halogen,
- 6) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_1\text{-C}_{10})\text{alkyl}$,
- 7) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkenyl}$,
- 8) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkynyl}$,
- 9) $(\text{C}=\text{O})_r\text{O}_s\text{aryl}$,
- 10) $(\text{C}=\text{O})_r\text{O}_s\text{heterocyclyl}$,

11) (C₀-C₆)alkyl-NR^aR^b, or

12) (C₁-C₆)heterocyclyl,

wherein r and s are independently 0 or 1, and said alkyl, alkenyl, alkynyl, aryl, and heterocyclyl is optionally substituted with one or more substituents selected from R⁷;

R⁴ is H, aryl or (C₁-C₆)alkyl;

R⁵ is:

- 1) H,
- 2) SO₂R^c,
- 3) (C=O)_rR^c, wherein r is 0 or 1, or
- 4) CO₂R^c;

R⁶ is:

- 1) [aryl] phenyl,
- 2) CN,
- 3) halogen,
- 4) [(C=O)NR^aR^b,]
- 5) [(C₁-C₁₀)alkyl,]
- 6) [(C₂-C₈)alkenyl,]
- 7) [(C₂-C₈)alkynyl,] or
- 8) heterocyclyl,

[wherein r and s are independently 0 or 1, and] said [aryl] phenyl[, alkyl, alkenyl, alkynyl] and heterocyclyl optionally substituted with one or more substituents selected from R⁷;

R⁷ is:

- 1) O_r(C=O)_sNR^aR^b,
- 2) (C=O)_rO_saryl,

- 3) $(\text{C}=\text{O})_r\text{O}_s\text{-heterocyclyl}$,
- 4) halogen,
- 5) OH,
- 6) oxo,
- 7) $\text{O}(\text{C}_1\text{-C}_3)\text{perfluoroalkyl}$,
- 8) $(\text{C}_1\text{-C}_3)\text{perfluoroalkyl}$,
- 9) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_1\text{-C}_6)\text{alkyl}$,
- 10) CHO,
- 11) CO_2H ,
- 12) CN,
- 13) $(\text{C}_1\text{-C}_6)\text{alkyl-NR}^a\text{R}^b$, or
- 14) $(\text{C}_1\text{-C}_6)\text{alkyl-heterocyclyl}$,

wherein r and s are independently 0 or 1, and said aryl, heterocyclyl and alkyl are optionally substituted with one to three substituents selected from R^d ;

~~R^a and R^b are independently~~

- 1) H ,
- 2) $(\text{C}=\text{O})_r(\text{C}_1\text{-C}_{10})\text{alkyl}$,
- 3) $\text{S}(\text{O})_2\text{R}^e$,
- 4) $(\text{C}=\text{O})_r\text{heterocyclyl}$,
- 5) $(\text{C}=\text{O})_r\text{aryl}$, or
- 6) CO_2R^e ,

~~wherein r is 0 or 1 and said alkyl, heterocyclyl, and aryl optionally substituted with one or more substituents selected from R^d , or~~

R^a and R^b are taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to

the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^d ;

R^c is (C₁-C₆)alkyl, aryl, or heterocyclyl; and

R^d is:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl, wherein r and s are independently 0 or 1, optionally substituted with up to three substituents selected from OH, (C₁-C₆)alkoxy, halogen, heterocyclyl, CN, oxo, $N(R^e)_2$ and $S(O)_2R^c$,
- 2) $O_r(C_1-C_3)$ perfluoroalkyl,
- 3) (C₀-C₆)alkylene- $S(O)_mR^c$, wherein m is 0, 1, or 2,
- 4) oxo,
- 5) OH,
- 6) halo,
- 7) CN,
- 8) (C₀-C₆)alkylene-aryl, optionally substituted with up to three substituents selected from R^e ,
- 9) (C₀-C₆)alkylene-heterocyclyl, optionally substituted with up to three substituents selected from R^e ,
- 10) $C(O)R^c$,
- 11) CO_2R^c ,
- 12) $C(O)H$,
- 13) $N(R^e)_2$, or
- 14) CO_2H ;

R^e is:

- 1) H,

- 2) (C₁-C₆)alkyl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C₁-C₆)alkoxy, halogen, CN, oxo, N(R^f)₂ and S(O)₂R^c,
- 3) aryl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C₁-C₆)alkoxy, halogen, CN, N(R^f)₂ and S(O)₂R^c,
- 4) heterocyclyl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C₁-C₆)alkoxy, halogen, CN, oxo, N(R^f)₂ and S(O)₂R^c, or
- 6) S(O)₂R^c, or

if two R^e's are on a nitrogen atom, they can be taken together with the nitrogen to form a heterocycle with 5-7 atoms, optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said heterocycle optionally substituted with one or more substituents selected from OH, (C₁-C₆)alkoxy, halogen, CN, oxo, N(R^f)₂ and S(O)₂R^c; and

R^f is H, aryl or (C₁-C₆)alkyl.

Claim 2 (currently amended): The compound of Claim 1, wherein

Y is S;

R¹ is H, (C₁-C₆)alkyl, or O(C₁-C₆)alkyl;

R² is:

- 1) H, provided that both R¹ and R² are not H at the same time,
- 2) O_r(C₁-C₆)perfluoroalkyl,
- 3) OH,
- 4) CN,
- 5) halogen,

- 6) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_1\text{-C}_{10})\text{alkyl}$,
- 7) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkenyl}$,
- 8) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkynyl}$,
- 9) $(\text{C}=\text{O})_r\text{O}_s\text{aryl}$,
- 10) $(\text{C}=\text{O})_r\text{O}_s\text{heterocyclyl}$,
- 11) $(\text{C}_0\text{-C}_6)\text{alkyl-NR}^a\text{R}^b$, or
- 12) $(\text{C}_1\text{-C}_6)\text{heterocyclyl}$,

wherein r and s are independently 0 or 1, and said alkyl, alkenyl, alkynyl, aryl, and heterocyclyl is optionally substituted with one or more substituents selected from R^7 ;

R^6 is:

- 1) [aryl] phenyl,
- 2) CN,
- 3) halogen,
- 4) $[(\text{C}=\text{O})\text{NR}^a\text{R}^b]$,
- 5) $[(\text{C}_1\text{-C}_6)\text{alkyl}]$,
- 6) $[(\text{C}_2\text{-C}_6)\text{alkenyl}]$,
- 7) $[(\text{C}_2\text{-C}_6)\text{alkynyl}]$ or
- 8) heterocyclyl,

[wherein r and s are independently 0 or 1, and] said [aryl] phenyl], alkyl, alkenyl, alkynyl] and heterocyclyl optionally substituted with one to three substituents selected from R^7 ;

R^7 is:

- 1) $\text{O}_r(\text{C}=\text{O})_s\text{NR}^a\text{R}^b$,
- 2) $(\text{C}=\text{O})_r\text{O}_s\text{aryl}$,
- 3) $(\text{C}=\text{O})_r\text{O}_s\text{-heterocyclyl}$,
- 4) halogen,
- 5) OH,

- 6) oxo,
- 7) $O(C_1-C_3)\text{perfluoroalkyl}$,
- 8) $(C_1-C_3)\text{perfluoroalkyl}$,
- 9) $(C=O)_rO_s(C_1-C_6)\text{alkyl}$,
- 10) CHO,
- 11) CO_2H ,
- 12) CN,
- 13) $(C_1-C_6)\text{alkyl}-NR^aR^b$, or
- 14) $(C_1-C_6)\text{alkyl-heterocyclyl}$,

wherein r and s are independently 0 or 1, and said aryl, heterocyclyl and alkyl are optionally substituted with one to three substituents selected from R^d ;

~~R^a and R^b are independently:~~

- 1) —H,
- 2) — $(C=O)_r(C_1-C_{10})\text{alkyl}$,
- 3) — $S(O)_2R^e$,
- 4) — $(C=O)_r\text{heterocyclyl}$,
- 5) — $(C=O)_r\text{aryl}$, or
- 6) — CO_2R^e ,

~~wherein r is 0 or 1 and said alkyl, heterocyclyl, and aryl optionally substituted with one or more substituents selected from R^d , or~~

R^a and R^b are taken together with the nitrogen to which they are attached to form a monocyclic 5-7 membered heterocycle optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said heterocycle optionally substituted with one to three substituents selected from R^d ; and

R^d is:

- 1) $(C=O)_rO_s(C_1-C_6)alkyl$, wherein r and s are independently 0 or 1, optionally substituted with up to three substituents selected from OH, $(C_1-C_6)alkoxy$, halogen, CN, oxo, $N(R^e)_2$ and $S(O)_2R^c$,
- 2) $O_r(C_1-C_3)perfluoroalkyl$,
- 3) $(C_0-C_6)alkylene-S(O)_mR^c$, wherein m is 0, 1, or 2,
- 4) oxo,
- 5) OH,
- 6) halo,
- 7) CN,
- 8) $(C_0-C_6)alkylene-aryl$, optionally substituted with up to three substituents selected from R^e ,
- 9) $(C_0-C_6)alkylene-heterocyclyl$, optionally substituted with up to three substituents selected from R^e ,
- 10) $(C_0-C_6)alkylene-N(R^e)_2$,
- 11) $C(O)R^c$,
- 12) CO_2R^c ,
- 13) $C(O)H$, or
- 14) CO_2H .

Claim 3 (original): The compound of Claim 2, wherein A and B are N; and R^6 is phenyl, halogen, CN, or pyridyl said phenyl and pyridyl optionally substituted with one to three substituents selected from R^7 .

Claim 4 (original): The compound of Claim 3 wherein R^1 is H and R^2 is $O_r(C_1-C_6)alkyl$, wherein r is 0 or 1, optionally substituted with one to three substituents selected from R^7 , or $(C_0-C_6)alkyl-NR^aR^b$.

Claim 5 (original): A compound selected from:

2-({6-[4-(2-morpholin-4-ylethyl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile;

2-({6-[4-(2-morpholin-4-yl-2-oxoethyl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile;

N-(*tert*-butyl)-2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)acetamide;

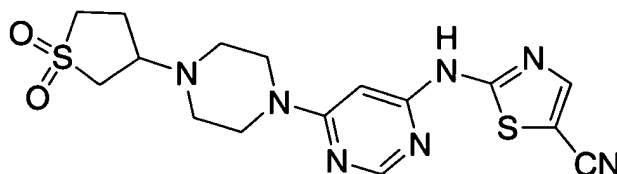
2-({6-[4-(1,1-dioxidotetrahydrothien-3-yl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile;

2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)-*N*-isopropylacetamide;

2-(1-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperidin-4-yl)-*N*-isopropylacetamide;
and

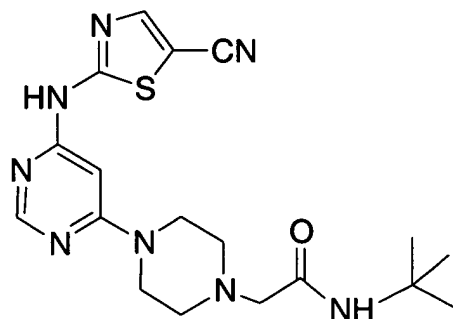
2-({6-[4-(2-oxopiperidin-3-yl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile;
or a pharmaceutically acceptable salt or stereoisomer thereof.

Claim 6 (original): A compound which is 2-({6-[4-(1,1-dioxidotetrahydrothien-3-yl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile



or a pharmaceutically acceptable salt or stereoisomer thereof.

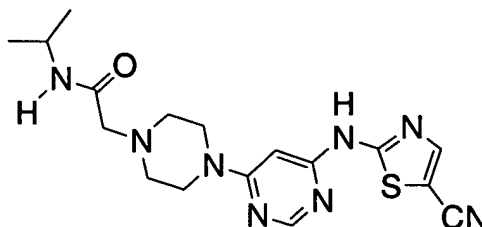
Claim 7 (original): A compound which is *N*-(*tert*-butyl)-2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)acetamide



or a pharmaceutically acceptable salt thereof.

Claim 8 (original): A compound which is the (R) or (S) enantiomer of 2-({6-[4-(1,1-dioxidotetrahydrothien-3-yl)piperazin-1-yl]pyrimidin-4-yl}amino)-1,3-thiazole-5-carbonitrile in enantiomerically pure form as characterized by an enantiomeric excess of at least 98%, or a pharmaceutically acceptable salt thereof.

Claim 9 (original): A compound which is 2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)-N-isopropylacetamide



or a pharmaceutically acceptable salt thereof.

Claim 10 (original): A pharmaceutical composition which is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

Claim 11 (canceled)

Claim 12 (currently amended): A method of treating cancer ~~or preventing cancer in accordance with Claim 11~~ in a mammal in need of such treatment which is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1, wherein ~~the~~ said cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

Claim 13 (currently amended): A method of treating cancer ~~or preventing cancer in accordance with Claim 11~~ in a mammal in need of such treatment which is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1, wherein ~~the~~ said

cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, glioblastomas and breast carcinoma.

Claim 14 (currently amended): A method of treating cancer ~~or preventing cancer in accordance with Claim 11~~ in a mammal in need of such treatment which is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1, wherein ~~the~~ said cancer is selected from colorectal cancer, prostate cancer, breast cancer, and lung cancer.

Claim 15 (currently amended): A method of treating ~~or preventing~~ a disease in which angiogenesis is implicated, said disease is an ocular disease, which is comprised of administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 16 (canceled)

Claim 17 (currently amended): A method of treating ~~or preventing~~ retinal vascularization which is comprised of administering to a mammal in need of such treatment a therapeutically effective amount of compound of Claim 1.

Claim 18 (currently amended): A method of treating ~~or preventing~~ diabetic retinopathy which is comprised of administering to a mammal in need of such treatment a therapeutically effective amount of compound of Claim 1.

Claim 19 (currently amended): A method of treating ~~or preventing~~ age-related macular degeneration which is comprised of administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 20 (original): The method of Claim 15 further comprising the use of photodynamic therapy with a photosensitive drug.

Claim 21 (original): The method of Claim 20 wherein the photosensitive drug is verteoporphin.

Claim 22 (original): The method of Claim 20 wherein the disease is age-related macular degeneration.

Claim 23 (currently amended): A method of treating ~~or preventing~~ inflammatory diseases said diseases selected from rheumatoid arthritis, psoriasis, contact dermatitis and delayed hypersensitivity reactions, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claims 24-25 (canceled)

Claim 26 (original): A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

Claim 27 (original): A process for making a pharmaceutical composition which comprises combining a compound of Claim 1 with a pharmaceutically acceptable carrier.

Claim 28 (currently amended): A method of treating ~~or preventing~~ bone associated pathologies selected from osteosarcoma, osteoarthritis, and rickets which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 29 (original): The composition of Claim 10 further comprising a second compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) retinoid receptor modulator,
- 4) a cytotoxic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,

- 9) a reverse transcriptase inhibitor,
- 10) another angiogenesis inhibitor, and
- 11) a PPAR- γ agonist.

Claim 30 (original): The composition of Claim 29, wherein the second compound is another angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, and an antibody to VEGF.

Claim 31 (original): The composition of Claim 29, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

Claim 32 (original): The composition of Claim 10 further comprising a steroidal anti-inflammatory compound.

Claim 33 (original): The composition of Claim 10 further comprising an anti-hypertensive compound.

Claims 34-39 (canceled)

Claim 40 (currently amended): A method of reducing ~~or preventing~~ tissue damage following a cerebral ischemic event which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claims 41-42 (canceled)

Claim 43 (currently amended): A method of treating ~~or preventing~~ tissue damage due to bacterial meningitis which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 44 (currently amended): A method to treat ~~or prevent~~ endometrioses which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 45 (currently amended): A method of treating ~~or preventing~~ diabetic retinopathy which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with a PPAR- γ agonist.

Claim 46 (currently amended): A method of treating acute myeloid leukemia which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

Claim 47 (currently amended): A method of treating cancer which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with gene therapy.